

September 15, 2008

Department of
Preventive Medicine

Nigel Fields, M.S.P.H.
Environmental Health Scientist
National Center for Environmental Research
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W. (8723F)
Washington, DC 20460-0001

RE: RD83186101, 2-year no cost extension request

Dear Mr. Fields:

In accordance with EPA guidelines, we are requesting a 2-year no cost extension for the "Children's Environmental Health Center" (PI: Gilliland, Grant No. RD83186101) to complete the proposed scope of work. During the grant period, two key investigators, Dr. Nino Kuenzli and Dr. David Diaz-Sanchez, transitioned to other universities or organizations. While they both remain actively involved in the center's activities and research projects, their departures have caused substantial delays in completing the original scope of work. We have ongoing analyses and manuscripts in preparation or planned for all three projects, follow-up meetings with our community partners and plans to disseminate the results to stake holders, and preparation of a video planned to update the community on results from the southern California Children's Health Study. We will use this extension to support staff to complete these critical tasks budgeted as part of the original scope of work. We anticipate that there will be approximately \$950,000 (total including indirect costs) remaining at the completion of the current budget year.

In the following paragraphs, we provide an update on the results and accomplishments of the three projects and two cores and highlight the plans to complete the proposed scope of work in the next two years.

Project 1: Urban Air Pollution, and Persistent Early Life Asthma

Questionnaire interviews have been completed in the asthma case-control study (with 75% participation). Analysis of the case-control data is puzzling, as the air pollution exposure predicted from models in the entire cohort is associated with asthma, but the conditional logistic analysis of measured air pollution exposure at homes of case-control is not. Analysis is ongoing to resolve this inconsistency and to finalize analyses and manuscript preparation. Genotyping has been completed and analyses of gene main effects and gene-air pollution analyses are underway.

A methods paper on the burden of disease in a Community Based Participatory Research (CBPR) partner community demonstrated that (conservatively) 8% of all childhood asthma in Long Beach can be attributed to local traffic exposure. A more comprehensive childhood burden of air pollution paper is being developed covering both of our partner communities and multiple respiratory outcomes as part of our community-based participatory research effort.

We have worked closely with CBPR partners so that all participating are well versed in the new science developing from these efforts. All press releases on important papers are coordinated so that community partners are well prepared to comment on relevance to local air pollution and traffic issues. This has been quite successful, and the collaboration with scientists and community partners has resulted in the results having greater relevance for policy. Community partners have been trained to use a tool kit for evaluating near road exposure.

Project 2: Pollution- Enhanced Allergic Inflammation and Phase II Enzymes

The principal finding of this last year is the close correlation between the capacity of an individual to produce Phase II enzymes and their airway inflammatory response to challenge with DEP. This supports the view that children are more susceptible to high levels of pollutants due to a diminished ability to form this protective antioxidant response. The discovery that *in vitro* GST expression is associated with *in vivo* inflammatory responses, provides the potential to develop a diagnostic test for susceptibility to oxidant pollutants.

We will complete study of adults and children during this 2-year extension and further develop an *in vitro* test to predict airway susceptibility to pollutants. We have several manuscripts in preparation based on our current results and there are several key manuscripts planned based on the results of final data analysis.

Project 3: Air Pollution, Exhaled Breath Markers, and Asthma in Susceptible Children

Exhaled NO (eNO) has the potential for use in understanding asthma etiology, for identifying high-risk children and for use as a marker of response in intervention studies. This program of innovative research builds on the results from studies in the initial five years of the Children's Environmental Health Center, the population resource of a large ongoing prospective cohort study of the determinants of childhood asthma incidence and an extensive cutting-edge air pollution exposure assessment program to efficiently fill key research and public health needs.

We have completed fieldwork for the eNO study. Buccal cells for DNA were collected, processed and stored in the Molecular Biology Core of the Southern California Environmental Health Sciences Center. We developed NOS assays and have completed genotyping. We are completing follow-up of the cohort for asthma status and exposure variables. A manuscript describing innovative methods used in this study has recently been accepted for publication. Analysis of the data are ongoing, and descriptive analyses of eNO determinants, distributed lag associations with air pollution, with incident asthma, and with genetic variants in iNOS, and gene-air pollution interactions are underway.

We expect that final cohort follow-up, additional data review and these complex analyses and associated papers will require an additional 2 years to complete.

Community Outreach and Translation Core

The COTC is ensuring that results of the scientific studies being conducted by Center investigators reaches the public, is considered in the public policy arena, and that the interests of the community are reflected in the CBPR project.

Several case studies of the CBPR/COTC collaborative activities are being developed for publication, including truck counting in Mira Loma and West Long Beach. We also plan to produce a documentary video based on research highlights from the Children's Environmental Health Center in 2004-2008.

Exposure Assessment and Modeling Core

The objectives of the Exposure Assessment and Modeling Core have been to (1) extend exposure assessment capabilities through the collection of ambient pollution measurements in sampling microenvironments of particular interest to project investigators in the Center; (2) deploy passive samplers in each of the 13 study communities to understand how pollutant levels vary locally, particularly with respect to proximity to roadways; and (3) utilize innovative modeling approaches to develop temporally and spatially resolved estimates of micro-environmental individual exposures.

All field work has been completed. Analyses are progressing nicely on the dependence of local variation in NO₂, NO, NO_x, and O₃ on traffic proximity, and on whether the relationship between traffic and local air quality is similar across our 13 communities. We have also investigated whether simple GIS measures (e.g. distance to a freeway) are as good at predicting local air quality as more complex measures (e.g. dispersion-based modeling of concentrations using the CALINE model). Our results indicate that the former simpler measures provide a good means of predicting local air quality, and we completing analyses for an exposure model that can be used not only within our 13 study communities, but more generally across southern California. A manuscript is under preparation.

Thank you for your consideration,

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Frank D. Gilliland, MD, PhD
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Lillian Rivera
Contract and Grant Administrator

Cc: Rich Callan